

What is claimed is:

- 5 1. An isolated nucleic acid encoding a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.
2. The nucleic acid of claim 1, wherein the nucleic acid is DNA.
- 10 3. The DNA of claim 2, wherein the DNA is cDNA.
4. The DNA of claim 2, wherein the DNA is genomic DNA.
- 15 5. The nucleic acid of claim 1, wherein the nucleic acid is RNA.
- 20 6. The nucleic acid of claim 1, wherein the human MCH1 receptor has an amino acid sequence identical to that encoded by the plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197).
- 25 7. The nucleic acid of claim 1, wherein the human MCH1 receptor comprises an amino acid sequence as shown in Figure 2 (SEQ ID NO: 2).
8. The nucleic acid of claim 1, wherein the mutant human MCH1 receptor comprises an amino acid sequence as shown in Figure 13 (SEQ ID NO: 26).
- 30 9. The nucleic acid of claim 1, wherein the mutant human MCH1 receptor comprises an amino acid sequence as shown in Figure 14 (SEQ ID NO: 27).
- 35 10. The nucleic acid of claim 1, wherein the mutant human

MCH1 receptor comprises an amino acid sequence as shown in Figure 15 (SEQ ID NO: 28).

11. A purified human MCH1 receptor protein.
12. A vector comprising the nucleic acid of claim 1.
13. The vector of claim 12 adapted for expression in a cell which comprises the regulatory elements necessary for expression of the nucleic acid in the cell operatively linked to the nucleic acid encoding the receptor so as to permit expression thereof, wherein the cell is a bacterial, amphibian, yeast, insect or mammalian cell.
14. The vector of claim 13, wherein the vector is a baculovirus.
15. The vector of claim 12, wherein the vector is a plasmid.
16. The plasmid of claim 15 designated pEXJ.HR-TL231 (ATCC Accession No. 203197).
17. A cell comprising the vector of claim 13.
18. A cell of claim 17, wherein the cell is a non-mammalian cell.
19. A cell of claim 18, wherein the non-mammalian cell is a *Xenopus* oocyte cell or a *Xenopus* melanophore cell.
20. A cell of claim 17, wherein the cell is a mammalian cell.

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21. A mammalian cell of claim 20, wherein the cell is a COS-7 cell, a 293 human embryonic kidney cell, a NIH-3T3 cell, a LM(tk-) cell, a mouse Y1 cell, or a CHO cell.
22. An insect cell comprising the vector of claim 13.
- 10 23. An insect cell of claim 22, wherein the insect cell is an Sf9 cell, an Sf21 cell or a Trichoplusia ni 5B-4 cell.
24. A membrane preparation isolated from the cell of claim 17.
- 15 25. A nucleic acid probe comprising at least 15 nucleotides which specifically hybridizes with a nucleic acid encoding a human MCH1 receptor, wherein the probe has a unique sequence corresponding to a sequence present within one of the two strands of the
- 20 nucleic acid encoding a human MCH1 receptor present in plasmid pEXJ.HR-T231 (ATCC Accession No. 203197).
- 25 26. A nucleic acid probe comprising at least 15 nucleotides which specifically hybridizes with a nucleic acid encoding a human MCH1 receptor, wherein the probe has a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence shown in Figure 1 (SEQ ID NO: 1) or (b) the reverse complement thereof.
- 30 27. The nucleic acid probe of claim 25 or 26, wherein the nucleic acid is DNA.
- 35 28. The nucleic acid probe of claim 25 or 26, wherein the nucleic acid is RNA.

29. An antisense oligonucleotide having a sequence capable of specifically hybridizing to the RNA of claim 5, so as to prevent translation of the RNA.
- 5 30. An antisense oligonucleotide having a sequence capable of specifically hybridizing to the genomic DNA of claim 4.
- 10 31. An antisense oligonucleotide of claim 29 or 30, wherein the oligonucleotide comprises chemically modified nucleotides or nucleotide analogues.
- 15 32. An antibody capable of binding to a human MCH1 receptor encoded by the nucleic acid of claim 1.
- 20 33. An agent capable of competitively inhibiting the binding of the antibody of claim 32 to a human MCH1 receptor.
- 25 34. An antibody of claim 32, wherein the antibody is a monoclonal antibody or antisera.
- 30 35. A pharmaceutical composition comprising (a) an amount of the oligonucleotide of claim 29 capable of passing through a cell membrane and effective to reduce expression of a human MCH1 receptor and (b) a pharmaceutically acceptable carrier capable of passing through the cell membrane.
- 35 36. A pharmaceutical composition of claim 35, wherein the oligonucleotide is coupled to a substance which inactivates mRNA.
37. A pharmaceutical composition of claim 36, wherein the substance which inactivates mRNA is a ribozyme.

- 5 38. A pharmaceutical composition of claim 35, wherein the pharmaceutically acceptable carrier comprises a structure which binds to a human MCH1 receptor on a cell capable of being taken up by the cells after binding to the structure.
- 10 39. A pharmaceutical composition of claim 35, wherein the pharmaceutically acceptable carrier is capable of binding to a human MCH1 receptor which is specific for a selected cell type.
- 15 40. A pharmaceutical composition which comprises an amount of the antibody of claim 32 effective to block binding of a ligand to a human MCH1 receptor and a pharmaceutically acceptable carrier.
- 20 41. A transgenic, nonhuman mammal expressing DNA encoding a human MCH1 receptor of claim 1.
- 25 42. A transgenic, nonhuman mammal comprising a homologous recombination knockout of the native human MCH1 receptor.
- 30 43. A transgenic, nonhuman mammal whose genome comprises antisense DNA complementary to the DNA encoding a human MCH1 receptor of claim 1 so placed within the genome as to be transcribed into antisense mRNA which is complementary to mRNA encoding the human MCH1 receptor and which hybridizes to mRNA encoding the human MCH1 receptor, thereby reducing its translation.
- 35 44. The transgenic, nonhuman mammal of claim 41 or 42, wherein the DNA encoding the human MCH1 receptor additionally comprises an inducible promoter.

45. The transgenic, nonhuman mammal of claim 41 or 42, wherein the DNA encoding the human MCH1 receptor additionally comprises tissue specific regulatory elements.

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46. A transgenic, nonhuman mammal of claim 41, 42, or 43, wherein the transgenic, nonhuman mammal is a mouse.

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47. A process for identifying a chemical compound which specifically binds to a mammalian MCH1 receptor which comprises contacting cells comprising DNA encoding, and expressing on their cell surface, the mammalian MCH1 receptor, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the mammalian MCH1 receptor, wherein the cells do not normally express the mammalian MCH1 receptor and the DNA encoding the mammalian MCH1 receptor (a) hybridizes to a nucleic acid having the defined sequence shown in Figure 1 (SEQ ID NO: 1) under low stringency conditions or a sequence complementary thereto and (b) is further characterized by its ability to cause a change in the pH of a culture of CHO cells when a MCH1 ligand is added to the culture and the CHO cells contain the nucleic acid which hybridized to the nucleic acid having the defined sequence or its complement.

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48. A process for identifying a chemical compound which specifically binds to a mammalian MCH1 receptor which comprises contacting a membrane preparation from cells comprising DNA encoding, and expressing on their cell surface, the mammalian MCH1 receptor, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the mammalian MCH1 receptor, wherein the cells do not

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normally express the mammalian MCH1 receptor and the DNA encoding the mammalian MCH1 receptor (a) hybridizes to a nucleic acid having the defined sequence shown in Figure 1 (SEQ ID NO: 1) under low stringency conditions or a sequence complementary thereto and (b) is further characterized by its ability to cause a change in the pH of a culture of CHO cells when a MCH1 ligand is added to the culture and the CHO cells contain the nucleic acid which hybridized to the nucleic acid having the defined sequence or its complement.

49. The process of claim 47 or 48, wherein the mammalian MCH1 receptor is a human MCH1 receptor.

50. The process of claim 47 or 48, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

51. The process of claim 47 or 48, wherein the mammalian MCH1 receptor has substantially the same amino acid sequence as the sequence of the human MCH1 receptor encoded by plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197).

52. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises substantially the same amino acid sequence as that shown in Figure 2 (SEQ ID NO: 2).

53. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises the amino acid sequence shown in Figure 2 (SEQ ID NO: 2).

54. The process of claim 47 or 48, wherein the mammalian MCH1 receptor comprises the amino acid sequence shown

in Figure 13 (SEQ ID NO: 26).

55. The process of claim 47 or 48, wherein the mammalian
MCH1 receptor comprises the amino acid sequence shown
5 in Figure 14 (SEQ ID NO: 27).

56. The process of claim 47 or 48, wherein the mammalian
MCH1 receptor comprises the amino acid sequence shown
10 in Figure 15 (SEQ ID NO: 28).

57. The process of claim 47 or 48, wherein the compound is
not previously known to bind to a mammalian MCH1
receptor.

15 58. A compound identified by the process of claim 57.

59. A process of claim 47 or 48, wherein the cell is an
insect cell.

20 60. The process of claim 47 or 48, wherein the cell is a
mammalian cell.

61. The process of claim 60, wherein the cell is
nonneuronal in origin.

25 62. The process of claim 61, wherein the nonneuronal cell
is a COS-7 cell, 293 human embryonic kidney cell, a
CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-
) cell.

30 63. A process of claim 60, wherein the compound is a
compound not previously known to bind to a mammalian
MCH1 receptor.

35 64. A compound identified by the process of claim 63.

65. A process involving competitive binding for
identifying a chemical compound which specifically
binds to a mammalian MCH1 receptor which comprises
contacting cells expressing on their cell surface the
mammalian MCH1 receptor, with both the chemical
compound and a second chemical compound known to bind
to the receptor, and separately with only the second
chemical compound, under conditions suitable for
binding of both compounds, and detecting specific
binding of the chemical compound to the mammalian MCH1
receptor, a decrease in the binding of the second
chemical compound to the mammalian MCH1 receptor in
the presence of the chemical compound indicating that
the chemical compound binds to the mammalian MCH1
receptor, wherein the cells do not normally express
the mammalian MCH1 receptor and the DNA encoding the
mammalian MCH1 receptor (a) hybridizes to a nucleic
acid having the defined sequence shown in Figure 1
(SEQ ID NO: 1) under low stringency conditions or a
sequence complementary thereto and (b) is further
characterized by its ability to cause a change in the
pH of a culture of CHO cells when a MCH1 ligand is
added to the culture and the CHO cells contain the
nucleic acid which hybridized to the nucleic acid
having the defined sequence or its complement.

66. A process involving competitive binding for
identifying a chemical compound which specifically
binds to a mammalian MCH1 receptor which comprises
contacting a membrane preparation from cells
expressing on their cell surface the mammalian MCH1
receptor, with both the chemical compound and a second
chemical compound known to bind to the receptor, and
separately with only the second chemical compound,
under conditions suitable for binding of both

compounds, and detecting specific binding of the chemical compound to the mammalian MCH1 receptor, a decrease in the binding of the second chemical compound to the mammalian MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the mammalian MCH1 receptor, wherein the cells do not normally express the mammalian MCH1 receptor and the DNA encoding the mammalian MCH1 receptor (a) hybridizes to a nucleic acid having the defined sequence shown in Figure 1 (SEQ ID NO: 1) under low stringency conditions or a sequence complementary thereto and (b) is further characterized by its ability to cause a change in the pH of a culture of CHO cells when a MCH1 ligand is added to the culture and the CHO cells contain the nucleic acid which hybridized to the nucleic acid having the defined sequence or its complement.

67. A process of claim 65 or 66, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

68. A process of claim 65 or 66, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

69. The process of claim 65 or 66, wherein the cell is an insect cell.

70. The process of claim 65 or 66, wherein the cell is a mammalian cell.

71. The process of claim 70, wherein the cell is nonneuronal in origin.

72. The process of claim 71, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.

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73. The process of claim 70, wherein the compound is not previously known to bind to a mammalian MCH1 receptor.

74. A compound identified by the process of claim 73.

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75. A method of screening a plurality of chemical compounds not known to bind to a mammalian MCH1 receptor to identify a compound which specifically binds to the mammalian MCH1 receptor, which comprises

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(a) contacting cells transfected with and expressing DNA encoding the mammalian MCH1 receptor with the plurality of compounds not known to bind specifically to the mammalian MCH1 receptor, under conditions permitting binding of compounds known to bind the mammalian MCH1 receptor;

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(b) determining whether the binding of a compound known to bind to the mammalian MCH1 receptor is reduced in the presence of the compounds within the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so

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(c) separately determining the binding to the mammalian MCH1 receptor of compounds included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the mammalian MCH1

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receptor.

76. A method of screening a plurality of chemical compounds not known to bind to a mammalian MCH1 receptor to identify a compound which specifically binds to the mammalian MCH1 receptor, which comprises

(a) contacting a membrane preparation from cells transfected with and expressing DNA encoding the mammalian MCH1 receptor with the plurality of compounds not known to bind specifically to the mammalian MCH1 receptor under conditions permitting binding of compounds known to bind the mammalian MCH1 receptor;

(b) determining whether the binding of a compound known to bind to the mammalian MCH1 receptor is reduced in the presence of the compounds within the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so

(c) separately determining the binding to the mammalian MCH1 receptor of compounds included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the mammalian MCH1 receptor.

77. A method of claim 75 or 76, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

78. A method of claim 75 or 76, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

5 79. A method of claim 75 or 76, wherein the cell is a mammalian cell.

80. A method of claim 79, wherein the mammalian cell is non-neuronal in origin.

10 81. The method of claim 80, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell, a CHO cell, a mouse Y1 cell, or an NIH-3T3 cell.

15 82. A method of detecting expression of a mammalian MCH1 receptor by detecting the presence of mRNA coding for the mammalian MCH1 receptor which comprises obtaining total mRNA from the cell and contacting the mRNA so obtained with the nucleic acid probe of any of claims
20 25, 26, 27, or 28 under hybridizing conditions, detecting the presence of mRNA hybridizing to the probe, and thereby detecting the expression of the mammalian MCH1 receptor by the cell.

25 83. A method of detecting the presence of a mammalian MCH1 receptor on the surface of a cell which comprises contacting the cell with the antibody of claim 32 under conditions permitting binding of the antibody to the receptor, detecting the presence of the antibody
30 bound to the cell, and thereby detecting the presence of the mammalian MCH1 receptor on the surface of the cell.

35 84. A method of determining the physiological effects of varying levels of activity of human MCH1 receptors

5 90. A method for identifying an agonist capable of
alleviating an abnormality in a subject wherein the
abnormality is alleviated by increasing the activity
of a human MCH1 receptor comprising administering a
compound to the transgenic, nonhuman mammal of claim
41, 44, 45, or 46, and determining whether the
compound alleviates the physical and behavioral
abnormalities displayed by the transgenic, nonhuman
mammal, the alleviation of the abnormality identifying
10 the compound as an agonist.

91. An agonist identified by the method of claim 90.

15 92. A pharmaceutical composition comprising an agonist of
claim 91 and a pharmaceutically acceptable carrier.

20 93. A method of treating an abnormality in a subject
wherein the abnormality is alleviated by increasing
the activity of a human MCH1 receptor which comprises
administering to the subject an effective amount of
the pharmaceutical composition of claim 92, thereby
treating the abnormality.

25 94. A method for diagnosing a predisposition to a disorder
associated with the activity of a specific mammalian
allele which comprises:

30 (a) obtaining DNA of subjects suffering from the
disorder;

(b) performing a restriction digest of the DNA
with a panel of restriction enzymes;

35 (c) electrophoretically separating the resulting
DNA fragments on a sizing gel;

(d) contacting the resulting gel with a nucleic acid probe capable of specifically hybridizing with a unique sequence included within the sequence of a nucleic acid molecule encoding a human MCH1 receptor and labeled with a detectable marker;

(e) detecting labeled bands which have hybridized to the DNA encoding a human MCH1 receptor of claim 1 labeled with a detectable marker to create a unique band pattern specific to the DNA of subjects suffering from the disorder;

(f) preparing DNA obtained for diagnosis by steps (a)-(e); and

(g) comparing the unique band pattern specific to the DNA of subjects suffering from the disorder from step (e) and the DNA obtained for diagnosis from step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to the disorder if the patterns are the same.

95. The method of claim 94, wherein a disorder associated with the activity of a specific mammalian allele is diagnosed.

96. A method of preparing the purified human MCH1 receptor of claim 11 which comprises:

(a) inducing cells to express the human MCH1 receptor;

(b) recovering the human MCH1 receptor from the induced cells; and

(c) purifying the human MCH1 receptor so recovered.

97. A method of preparing the purified human MCH1 receptor of claim 11 which comprises:

(a) inserting nucleic acid encoding the human MCH1 receptor in a suitable vector;

(b) introducing the resulting vector in a suitable host cell;

(c) placing the resulting cell in suitable condition permitting the production of the isolated human MCH1 receptor;

(d) recovering the human MCH1 receptor produced by the resulting cell; and

(e) purifying the human MCH1 receptor so recovered.

98. A process for determining whether a chemical compound is a mammalian MCH1 receptor agonist which comprises contacting cells transfected with and expressing DNA encoding the mammalian MCH1 receptor with the compound under conditions permitting the activation of the mammalian MCH1 receptor, and detecting an increase in mammalian MCH1 receptor activity, so as to thereby determine whether the compound is a mammalian MCH1 receptor agonist.

99. A process for determining whether a chemical compound is a mammalian MCH1 receptor antagonist which comprises contacting cells transfected with and expressing DNA encoding the mammalian MCH1 receptor with the compound in the presence of a known mammalian MCH1 receptor agonist, under conditions permitting the activation of the mammalian MCH1 receptor, and detecting a decrease in mammalian MCH1 receptor activity, so as to thereby determine whether the compound is a mammalian MCH1 receptor antagonist.

100. A process of claim 98 or 99, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

101. A process of claim 98 or 99, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

102. A pharmaceutical composition which comprises an amount of a mammalian MCH1 receptor agonist determined by the process of claim 98 effective to increase activity of a mammalian MCH1 receptor and a pharmaceutically acceptable carrier.

103. A pharmaceutical composition of claim 102, wherein the mammalian MCH1 receptor agonist is not previously known.

104. A pharmaceutical composition which comprises an amount of a mammalian MCH1 receptor antagonist determined by the process of claim 99 effective to reduce activity of a mammalian MCH1 receptor and a pharmaceutically acceptable carrier.

105. A pharmaceutical composition of claim 104, wherein the mammalian MCH1 receptor antagonist is not previously known.

5 106. A process for determining whether a chemical compound specifically binds to and activates a mammalian MCH1 receptor, which comprises contacting cells producing a second messenger response and expressing on their cell surface the
10 mammalian MCH1 receptor, wherein such cells do not normally express the mammalian MCH1 receptor, with the chemical compound under conditions suitable for activation of the mammalian MCH1 receptor, and measuring the second messenger response in the
15 presence and in the absence of the chemical compound, a change in the second messenger response in the presence of the chemical compound indicating that the compound activates the mammalian MCH1 receptor.

20 107. The process of claim 106, wherein the second messenger response comprises chloride channel activation and the change in second messenger is an increase in the level of inward chloride
25 current.

108. A process for determining whether a chemical compound specifically binds to and inhibits activation of a mammalian MCH1 receptor, which
30 comprises separately contacting cells producing a second messenger response and expressing on their cell surface the mammalian MCH1 receptor, wherein such cells do not normally express the mammalian MCH1 receptor, with both the chemical compound and
35 a second chemical compound known to activate the

mammalian MCH1 receptor, and with only the second chemical compound, under conditions suitable for activation of the mammalian MCH1 receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the mammalian MCH1 receptor.

109. The process of claim 108, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

110. A process of any of claims 106, 107, 108, or 109, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

111. A process of any of claims 106, 107, 108, or 109, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

112. The process of any of claims 106, 107, 108, 109, or 110, wherein the cell is an insect cell.

121. A pharmaceutical composition of claim 120, wherein the mammalian MCH1 receptor antagonist is not previously known.

5 122. A method of screening a plurality of chemical compounds not known to activate a mammalian MCH1 receptor to identify a compound which activates the mammalian MCH1 receptor which comprises:

10 (a) contacting cells transfected with and expressing the mammalian MCH1 receptor with the plurality of compounds not known to activate the mammalian MCH1 receptor, under conditions permitting activation of the
15 mammalian MCH1 receptor;

(b) determining whether the activity of the mammalian MCH1 receptor is increased in the presence of the compounds; and if so
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(c) separately determining whether the activation of the mammalian MCH1 receptor is increased by each compound included in the plurality of compounds, so as to thereby identify the
25 compound which activates the mammalian MCH1 receptor.

123. A method of claim 122, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of
30 such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

124. A method of claim 122, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.
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125. A method of screening a plurality of chemical compounds not known to inhibit the activation of a mammalian MCH1 receptor to identify a compound which inhibits the activation of the mammalian MCH1 receptor, which comprises:

(a) contacting cells transfected with and expressing the mammalian MCH1 receptor with the plurality of compounds in the presence of a known mammalian MCH1 receptor agonist, under conditions permitting activation of the mammalian MCH1 receptor;

(b) determining whether the activation of the mammalian MCH1 receptor is reduced in the presence of the plurality of compounds, relative to the activation of the mammalian MCH1 receptor in the absence of the plurality of compounds; and if so

(c) separately determining the inhibition of activation of the mammalian MCH1 receptor for each compound included in the plurality of compounds, so as to thereby identify the compound which inhibits the activation of the mammalian MCH1 receptor.

126. A method of claim 125, wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

127. A method of claim 125, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

128. A method of any of claims 123, 124, 125, 126, or 127, wherein the cell is a mammalian cell.
129. A method of claim 128, wherein the mammalian cell is non-neuronal in origin.
130. The method of claim 129, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell or an NIH-3T3 cell.
131. A pharmaceutical composition comprising a compound identified by the method of claim 123 or 124 effective to increase mammalian MCH1 receptor activity and a pharmaceutically acceptable carrier.
132. A pharmaceutical composition comprising a compound identified by the method of claim 125 or 126 effective to decrease mammalian MCH1 receptor activity and a pharmaceutically acceptable carrier.
133. A method of treating an abnormality in a subject wherein the abnormality is alleviated by increasing the activity of a mammalian MCH1 receptor which comprises administering to the subject an amount of a compound which is a mammalian MCH1 receptor agonist effective to treat the abnormality.
134. A method of claim 133, wherein the abnormality is a regulation of a steroid or pituitary hormone disorder, an epinephrine release disorder, a gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder,

hypertension, diabetes, a respiratory disorder, asthma, a reproductive function disorder, an immune disorder, an endocrine disorder, a musculoskeletal disorder, a neuroendocrine disorder, a cognitive disorder, a memory disorder, a sensory modulation and transmission disorder, a motor coordination disorder, a sensory integration disorder, a motor integration disorder, a dopaminergic function disorder, a sensory transmission disorder, an olfaction disorder, a sympathetic innervation disorder, pain, psychotic behavior, morphine tolerance, opiate addiction, an affective disorder, a stress-related disorder, a fluid-balance disorder, a seizure disorder, or migraine.

135. A method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a mammalian MCH1 receptor which comprises administering to the subject an amount of a compound which is a mammalian MCH1 receptor antagonist effective to treat the abnormality.

136. A method of claim 135, wherein the abnormality is a regulation of a steroid or pituitary hormone disorder, an epinephrine release disorder, a gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder, hypertension, diabetes, a respiratory disorder, asthma, a reproductive function disorder, an immune disorder, an endocrine disorder, a musculoskeletal disorder, a neuroendocrine disorder, a cognitive disorder, a memory disorder, a sensory modulation and transmission disorder, a

motor coordination disorder, a sensory integration disorder, a motor integration disorder, a dopaminergic function disorder, a sensory transmission disorder, an olfaction disorder, a sympathetic innervation disorder, pain, psychotic behavior, morphine tolerance, opiate addiction, an affective disorder, a stress-related disorder, a fluid-balance disorder, a seizure disorder, or migraine.

137. A process for making a composition of matter which specifically binds to a mammalian MCH1 receptor which comprises identifying a chemical compound using the process of any of claims 47, 48, 65, 66, 75, or 76 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

138. A process for making a composition of matter which specifically binds to a mammalian MCH1 receptor which comprises identifying a chemical compound using the process of any of claims 98, 106, or 122 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

139. A process for making a composition of matter which specifically binds to a mammalian MCH1 receptor which comprises identifying a chemical compound using the process of any of claims 99, 108, or 125 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

140. The process of any of claims 137, 138, or 139,

wherein the mammalian MCH1 receptor is a human MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

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141. The process of any of claims 137, 138, or 139, wherein the mammalian MCH1 receptor is a human MCH1 receptor.

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142. A process for preparing a composition which comprises admixing a pharmaceutically acceptable carrier and a therapeutically effective amount of a chemical compound identified by the process of any of claims 47, 48, 65, 66, 75, or 76 or a novel structural and functional analog or homolog thereof.

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143. A process for preparing a composition which comprises admixing a pharmaceutically acceptable carrier and a therapeutically effective amount of a chemical compound identified by the process of any of claims 98, 106, or 122 or a novel structural and functional analog or homolog thereof.

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144. A process for preparing a composition which comprises admixing a pharmaceutically acceptable carrier and a therapeutically effective amount of a chemical compound identified by the process of any of claims 99, 108, or 125 or a novel structural and functional analog or homolog thereof.

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145. The process of any of claims 142, 143, or 144, wherein the mammalian MCH1 receptor is a human

MCH1 receptor or a mutant of such human MCH1 receptor which is activated by MCH or an analog or homolog thereof.

5 146. The process of any of claims 142, 143, or 144, wherein the mammalian MCH1 receptor is a rat MCH1 receptor.

10 147. A process for determining whether a chemical compound is a human MCH1 receptor antagonist which comprises contacting cells transfected with and expressing DNA encoding the human MCH1 receptor with the compound in the presence of a known human MCH1 receptor agonist, under conditions permitting the activation of the human MCH1 receptor, and detecting a decrease in human MCH1 receptor activity, so as to thereby determine whether the compound is a human MCH1 receptor antagonist, wherein the DNA encoding the human MCH1 receptor comprises the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), the known human MCH1 receptor agonist is MCH or a homolog or analog of MCH, and the cells do not express the MCH1 receptor prior to transfecting them.

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30 148. A process for determining whether a chemical compound specifically binds to and inhibits activation of a human MCH1 receptor, which comprises separately contacting cells expressing on their cell surface the human MCH1 receptor and producing a second messenger response upon activation of the human MCH1 receptor, wherein such cells do not normally express the human MCH1 receptor and the DNA encoding the human MCH1

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receptor comprises the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), with both the chemical compound and a second chemical compound known to activate the human MCH1 receptor, and with only the second chemical compound, under conditions suitable for activation of the human MCH1 receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the human MCH1 receptor, wherein the second chemical compound is MCH or a homolog or analog of MCH.

149. The process of claim 148, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

150. A method of screening a plurality of chemical compounds not known to inhibit the activation of a human MCH1 receptor to identify a compound which inhibits the activation of the human MCH1 receptor, which comprises:

(a) contacting cells transfected with and expressing the human MCH1 receptor, wherein such cells do not normally express the human MCH1 receptor and the DNA encoding the human MCH1 receptor comprises the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), with the plurality of compounds in the presence of a known human MCH1 receptor agonist, under conditions permitting activation of the human MCH1 receptor, wherein the known MCH1 receptor agonist is MCH or a homolog or analog of MCH;

(b) determining whether the activation of the human MCH1 receptor is reduced in the presence of the plurality of compounds, relative to the activation of the human MCH1 receptor in the absence of the plurality of compounds; and if so

(c) separately determining the extent of inhibition of activation of the human MCH1 receptor for each compound included in the plurality of compounds, so as to thereby identify the compound which inhibits the activation of the human MCH1 receptor.

151. The process of any of claims 147, 148 or 150, wherein the cell is an insect cell.

152. The process of any of claims 147, 148 or 150, wherein the cell is a mammalian cell.

153. The process of any of claims 147, 148 or 150,

wherein the cell is a mammalian cell which is nonneuronal in origin.

- 5 154. The process of any of claims 147, 148 or 150, wherein the cell is a COS-7 cell, a CHO cell, a 293 human embryonic kidney cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.
- 10 155. A process for making a composition of matter which specifically binds to a human MCH1 receptor which comprises identifying a chemical compound which specifically binds to the human MCH1 receptor and then synthesizing the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting the extent of specific binding of the chemical compound to the human MCH1 receptor, a decrease in the binding of the second chemical compound to the human MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the human MCH1 receptor, wherein the cells do not normally express the human MCH1 receptor, the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the second chemical compound is
- 15 20 25 30 35

105020" 2E266550

MCH or a homolog or analog of MCH.

156. A process for making a composition of matter which specifically binds to a human MCH1 receptor which comprises identifying a chemical compound which specifically binds to the human MCH1 receptor and then synthesizing the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting a membrane preparation from cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting the extent of specific binding of the chemical compound to the human MCH1 receptor, a decrease in the binding of the second chemical compound to the human MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the human MCH1 receptor, wherein the cells do not normally express the human MCH1 receptor, the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the second chemical compound is MCH or a homolog or analog of MCH.

157. A process for making a composition of matter which is a human MCH1 receptor antagonist which comprises identifying a chemical compound which is

5 a human MCH1 receptor antagonist and then
synthesizing the chemical compound or a structural
and functional analog or homolog thereof, wherein
the chemical compound is identified as a human
MCH1 receptor antagonist by a process which
comprises contacting cells transfected with and
expressing DNA encoding the human MCH1 receptor
with the compound in the presence of a known human
MCH1 receptor agonist, under conditions permitting
10 the activation of the human MCH1 receptor, and
detecting a decrease in human MCH1 receptor
activity, so as to thereby determine whether the
compound is a human MCH1 receptor antagonist,
wherein the cells do not normally express the
human MCH1 receptor, the human MCH1 receptor is
15 encoded by nucleic acid comprising the sequence
shown in Figure 1 (Seq. ID No. 1) or contained in
plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197),
and the known human MCH1 receptor agonist is MCH
or a homolog or analog of MCH.
20

158. A process for making a composition of matter which
specifically binds to and inhibits the activation
of a human MCH1 receptor which comprises
25 identifying a chemical compound which specifically
binds to and inhibits the activation of the human
MCH1 receptor and then synthesizing the chemical
compound or a structural and functional analog or
homolog thereof, wherein the chemical compound is
30 identified as binding to and inhibiting the
activation of the human MCH1 receptor by a process
which comprises separately contacting cells
expressing on their cell surface the human MCH1
receptor and producing a second messenger response
35 upon activation of the human MCH1 receptor,

wherein such cells do not normally express the human MCH1 receptor and the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), with both the chemical compound and a second chemical compound known to activate the human MCH1 receptor, and with only the second chemical compound, under conditions suitable for activation of the human MCH1 receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the human MCH1 receptor, wherein the second chemical compound is MCH or a homolog or analog of MCH.

159. The process of claim 158, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

160. A process for preparing a composition which comprises identifying a chemical compound which specifically binds to a human MCH1 receptor, and then admixing a carrier and the chemical compound

or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and separately with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting the extent of specific binding of the chemical compound to the human MCH1 receptor, a decrease in the binding of the second chemical compound to the human MCH1 receptor in the presence of the chemical compound indicating that the chemical compound binds to the human MCH1 receptor, wherein the cells do not normally express the human MCH1 receptor, the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the second chemical compound is MCH or a homolog or analog of MCH.

161. A process for preparing a composition which comprises identifying a chemical compound which specifically binds to a human MCH1 receptor, and then admixing a carrier and the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to the human MCH1 receptor by a process involving competitive binding which comprises contacting a membrane preparation from cells expressing on their cell surface the human MCH1 receptor, with both the chemical compound and

5 a second chemical compound known to bind to the
receptor, and separately with only the second
chemical compound, under conditions suitable for
binding of both compounds, and detecting the
extent of specific binding of the chemical
10 compound to the human MCH1 receptor, a decrease in
the binding of the second chemical compound to the
human MCH1 receptor in the presence of the
chemical compound indicating that the chemical
compound binds to the human MCH1 receptor, wherein
the cells do not normally express the human MCH1
receptor, the human MCH1 receptor is encoded by
nucleic acid comprising the sequence shown in
Figure 1 (Seq. ID No. 1) or contained in plasmid
15 pEXJ.HR-TL231 (ATCC Accession No. 203197), and the
second chemical compound is MCH or a homolog or
analog of MCH.

162. 20 A process for preparing a composition which
comprises identifying a chemical compound which is
a human MCH1 receptor antagonist, and then
admixing a carrier and the chemical compound or a
structural and functional analog or homolog
thereof, wherein the chemical compound is
25 identified as a human MCH1 receptor antagonist by
a process which comprises contacting cells
transfected with and expressing DNA encoding the
human MCH1 receptor with the compound in the
presence of a known human MCH1 receptor agonist,
30 under conditions permitting the activation of the
human MCH1 receptor, and detecting a decrease in
human MCH1 receptor activity, so as to thereby
determine whether the compound is a human MCH1
receptor antagonist, wherein the cells do not
35 normally express the human MCH1 receptor, the

human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), and the known human MCH1 receptor agonist is MCH or a homolog or analog of MCH.

163. A process for preparing a composition which comprises identifying a chemical compound which specifically binds to and inhibits the activation of a human MCH1 receptor, and then admixing a carrier and the chemical compound or a structural and functional analog or homolog thereof, wherein the chemical compound is identified as binding to and inhibiting activation of the human MCH1 receptor by a process which comprises separately contacting cells expressing on their cell surface the human MCH1 receptor and producing a second messenger response upon activation of the human MCH1 receptor, wherein such cells do not normally express the human MCH1 receptor and the human MCH1 receptor is encoded by nucleic acid comprising the sequence shown in Figure 1 (Seq. ID No. 1) or contained in plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197), with both the chemical compound and a second chemical compound known to activate the human MCH1 receptor, and with only the second chemical compound, under conditions suitable for activation of the human MCH1 receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the

second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the human MCH1 receptor, wherein the second chemical compound is MCH or a homolog or analog of MCH.

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164. The process of claim 163, wherein the second messenger response comprises chloride channel activation and the change in second messenger response is a smaller increase in the level of inward chloride current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

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165. The process of any of claims 155, 156, 157, 158, 160, 161, 162, or 163, wherein the cell is an insect cell.

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166. The process of any of claims 155, 156, 157, 158, 160, 161, 162, or 163, wherein the cell is a mammalian cell.

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167. The process of claim 166, wherein the mammalian cell is nonneuronal in origin.

30

168. The process of claim 167, wherein the nonneuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.

35

169. A method of treating an eating disorder or obesity in a subject which comprises administering to the subject a therapeutically effective amount of an MCH1 antagonist which inhibits the activation of

the MCH1 receptor.

170. A method of claim 169, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 30-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the 5-HT2C and MC-4 receptors.

171. A method of claim 170, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 10-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

172. A method of claim 170, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 100-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the 5-HT2C and MC-4 receptors.

173. A method of claim 172, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 100-fold greater than the antagonist potency with which the MCH1 antagonist inhibits the activation of each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

174. A method of claim 169, wherein the MCH1 antagonist

additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 30-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the 5-HT2C and MC-4 receptors.

175. A method of claim 174, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 10-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

176. A method of claim 174, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the 5-HT2C and MC-4 receptors.

177. A method of claim 176, wherein the MCH1 antagonist additionally inhibits the activation of the MCH1 receptor with an antagonist potency which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

178. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 30-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the 5-HT2C and MC-4 receptors.

179. A method of claim 178, wherein the MCH1 antagonist

additionally binds to the MCH1 receptor with a binding affinity which is at least 10-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

180. A method of claim 178, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the 5-HT2C and MC-4 receptors.

181. A method of claim 180, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

182. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 30-fold greater than the binding affinity with which the MCH1 antagonist binds to the dopamine D2 receptor.

183. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 30-fold greater than the binding affinity with which the MCH1 antagonist binds to the histamine H1 receptor.

184. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold

greater than the binding affinity with which the MCH1 antagonist binds to the dopamine D2 receptor.

185. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to the histamine H1 receptor.
186. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 200-fold greater than the binding affinity with which the MCH1 antagonist binds to the dopamine D2 receptor.
187. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 200-fold greater than the binding affinity with which the MCH1 antagonist binds to the histamine H1 receptor.
188. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 10-fold greater than the binding affinity with which the MCH1 antagonist binds to the α_{1A} adrenoceptor.
189. A method of claim 169, wherein the MCH1 antagonist additionally binds to the MCH1 receptor with a binding affinity which is at least 100-fold greater than the binding affinity with which the MCH1 antagonist binds to the α_{1A} adrenoceptor.

190. A method of claim 169, wherein the MCH1 antagonist additionally binds to the α_{1A} adrenoceptor with a binding affinity which is no more than 10-fold greater than the binding affinity with which the MCH1 antagonist binds to the MCH1 receptor.

191. A method of claim 169, wherein the MCH1 antagonist additionally binds to the α_{1A} adrenoceptor with a binding affinity which is no more than 100-fold greater than the binding affinity with which the MCH1 antagonist binds to the MCH1 receptor.

192. A method of treating an eating disorder in a subject which comprises administering to the subject a therapeutically effective amount of an MCH1 agonist which activates the MCH1 receptor.

193. A method of claim 192, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 30-fold greater than the agonist potency with which the MCH1 agonist activates each of the 5-HT_{2C} and MC-4 receptors.

194. A method of claim 193, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 10-fold greater than the agonist potency with which the MCH1 agonist activates each of the NPY₁, NPY₅, GALR₁, GALR₂, and GALR₃ receptors.

195. A method of claim 193, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 100-fold greater than the agonist potency with which the MCH1

agonist activates each of the 5-HT_{2C} and MC-4 receptors.

196. A method of claim 195, wherein the MCH1 agonist additionally activates the MCH1 receptor with an agonist potency which is at least 100-fold greater than the agonist potency with which the MCH1 agonist activates each of the NPY1, NPY5, GALR1, GALR2, and GALR3 receptors.

197. A method of any one of claims 192, 193, 194, 195, or 196, wherein the eating disorder is anorexia nervosa.

198. A method of treating depression and/or anxiety in a subject which comprises administering to the subject a composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a MCH1 antagonist, wherein:

- (a) (1) the MCH1 antagonist does not inhibit the activity of central monoamine oxidase A greater than 50 percent, at a concentration of 10mM; and
(2) the MCH1 antagonist does not inhibit the activity of central monoamine oxidase B greater than 50 percent, at a concentration of 10mM; and
- (b) the MCH1 antagonist binds to the MCH1 receptor with a binding affinity at least ten-fold higher than the binding affinity with which it binds to each of the following transporters: serotonin transporter, norepinephrine transporter, and dopamine transporter.

199. The method of claim 198, wherein the MCH1 antagonist also binds to the MCH1 receptor with a binding

affinity at least ten-fold higher than the binding
affinity with which it binds to each of the human
5HT_{1A}, human 5HT_{1B}, human 5HT_{1D}, human 5HT_{1F}, human
5HT_{1F}, human 5HT_{2A}, rat 5HT_{2C}, human 5HT₄, human 5HT₆
and human 5HT₇ receptors.

200. The method of claim 198, wherein the MCH1 antagonist
also binds to the MCH1 receptor with a binding
affinity at least ten-fold higher than the binding
affinity with which it binds to the human histamine
H₁ and H₂ receptors.

201. The method of claim 198, wherein the MCH1 antagonist
also binds to the MCH1 receptor with a binding
affinity at least ten-fold higher than the binding
affinity with which it binds to the human dopamine D₁,
D₂, D₃, D₄ and D₅ receptors.

202. The method of claim 198, wherein the MCH1 antagonist
also binds to the MCH1 receptor with a binding
affinity at least ten-fold higher than the binding
affinity with which it binds to the human α_{1A}
adrenoceptor, the human α_{1B} adrenoceptor and the human
 α_{1D} adrenoceptor.

203. The method of claim 198, wherein the MCH1 antagonist
also binds to the MCH1 receptor with a binding
affinity at least ten-fold higher than the binding
affinity with which it binds to the human α_{2A}
adrenoceptor, the human α_{2B} adrenoceptor and the human
 α_{2C} adrenoceptor.

204. The method of claim 198, wherein the MCH1 antagonist
does not inhibit the activity of central monoamine
oxidase A greater than 60 percent.

205. The method of claim 198, wherein the MCH1 antagonist
does not inhibit the activity of central monoamine
oxidase B greater than 60 percent.
- 5 206. The method of claim 198, wherein the MCH1 antagonist
does not inhibit the activity of central monoamine
oxidase A greater than 70 percent.
- 10 207. The method of claim 198, wherein the MCH1 antagonist
does not inhibit the activity of central monoamine
oxidase B greater than 70 percent.

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